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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/674,803

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Robert Zelle

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EXAMINER

GRAHAM, SHELLEY R

ART UNIT

PAPER NUMBER

4173

MAIL DATE

DELIVERY MODE

11/27/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/674,803	Applicant(s) ZELLE ET AL.	
	Examiner Shelley R. Graham	Art Unit 4173	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☐ Claim(s) 1-24 is/are pending in the application.
 4a) Of the above claim(s) 5,8-13,16 and 18-24 is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☐ Claim(s) 1-4, 6, 7, 14, 15, and 17 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. ____. |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>1 page</u> . | 6) <input type="checkbox"/> Other: ____. |

DETAILED ACTION

Election/Restriction

1. Applicant's election of Group I, Claims 1-19, and the compound of formula (VI) with traverse, in the reply filed on 31 August 2007 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).
2. Claims 5, 8-13, 16, and 18-24 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as they do not read on the elected species and there being no allowable generic or linking claim. No claims have been amended, added or canceled. Accordingly, claims 1-4, 6, 7, 14, 15, and 17 are examined on the merits herewith.
3. The restriction requirement is made final.

Information Disclosure Statement

4. Receipt of one information disclosure statement filed by Applicants on 22 February 2006 is acknowledged. The references cited therein have been considered.

Objections

Specification:

5. The disclosure is objected to because of the following informalities: Page 8, formula (VIII) recites a definition for R^3 , however, there is no R^3 present in the structure formula (VIII).

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Claims:

6. Claim 15 is objected to because of the following informalities: The substituent (R_2) of formula (VIII) should read (R^2), consistent with the rest of the structure labels and the subsequent definitions.

Claim Rejections - 35 U.S.C. § 112 2nd

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claim Rejections - 35 U.S.C. § 112, 2nd

7. Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

8. It is unclear the definition of “Y” when “m” is 2. The way the claim is worded, Y must be only one of “H, OH, NH₂, or an organic moiety of C₁-C₂₀, optionally additionally containing 1-8 heteroatoms selected from the group consisting of N, P, O, S and halo”. According to the claim, if there are two Ys present in the formula, they must both be of equal value. However, the structure of the elected species has two independent values for Y.

Claim Rejections - 35 U.S.C. § 112, 2nd

9. Claim 7 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

10. It is unclear if the phrase “optionally substituted by oxo at the C adjacent N when n is 0 and Y is Φ_2CH ” further defines only the “divalent or trivalent straight-chain alkenylene (C3-C10)” or both the “divalent or trivalent straight-chain alkylene (C3-C10)” and the “divalent or trivalent straight-chain alkenylene (C3-C10)”. The same holds true for the (C5-C10) portion of the claim.

Claim Rejections - 35 U.S.C. § 112, 2nd

11. Claim 15 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

12. Claim 15 recites a definition for R^3 , n, and 1^3 , however, these groups are not present in the structure of formula (VIII).

Claim Rejections - 35 U.S.C. § 112, 2nd

13. Claim 16 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

14. Claim 16 recites a definition for R^3 , however, there is no R^3 group is not present in the structure of formula (VIII).

Claim Rejections - 35 U.S.C. § 112 1st

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

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pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

15. Claims 1-4, 6, 7, 14, 15, and 17 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for modulating human N-type calcium channel $\alpha_{1B+SFVG}$ subunit activity using the compounds 1 and 2, does not reasonably provide enablement for modulating human N-type calcium channel $\alpha_{1B+SFVG}$ subunit activity using any of the claimed compounds. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

16. The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: the nature of the invention; the state of the prior art; the relative skill of those in the art; the predictability or unpredictability of the art; the breadth of the claims; the amount of direction or guidance presented; the presence or absence of working examples; and the quantity of experimentation necessary. When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

17. The present invention is drawn to methods of modulating human N-type calcium channel $\alpha_{1B+SFVG}$ subunit activity, comprising administering an effective amount of a compounds of claims 1-4, 6, 7, 14, 15, and 17. Specifically, formulas I-VI, and IX.

18. The specification only discloses working examples for two compounds. Given under the subheading "Example", page 24, line 21, is IC50 data from an assay preformed using various

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calcium channels, whereby the modulation of the calcium channel is measured for each compound. The table includes data for compounds 1 and 2, only.

19. It is generally recognized in the art that biological compounds often react unpredictably under different circumstances (Nationwide Chem. Corp. v. Wright, 458 F. supp. 828, 839, 192 USPQ 95, 105(M.D. Fla. 1976); Aff'd 584 F.2d 714, 200 USPQ 257 (5th Cir. 1978); In re Fischer, 427 F.2d 833, 839, 166 USPQ 10, 24(CCPA 1970)). The relative skill of the artisan or the unpredictability of the pharmaceutical art is very high. Where the physiological activity of a chemical or biological compound is considered to be an unpredictable art (Note that in cases involving physiological activity such as the instant case, "the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved" (See In re fischer, 427 F.2d 833, 839, 166 USPQ 10, 24(CCPA 1970))), the skilled artisan would have not known how to extrapolate the results provided in the instant claims to the larger and varied genus of compounds claimed. For example, the structure of compound 1 has peripheral groups of methoxy-benzene and fluoro-benzenes, while compound 2 has benzyl and phenyl peripheral groups. However, the claimed formulae include a variety of peripheral groups, for example, tricycles, heteroaromatic rings, phenyl rings substituted with cyano or nitro groups, and aliphatic cyclic rings. The specification of the instant application has not provided guidance, working examples or mechanisms of action for the modulation of human N-type calcium channel $\alpha_{1B}+\text{SFVG}$ subunit activity for the wide variety of compounds claimed.

20. The examiner acknowledges that the Office does not require the presence of working examples in the disclosure of the invention (see MPEP 2164.02). However, given the highly unpredictable state of the art and furthermore, given that the applicant does not provide sufficient

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guidance or direction as to how to make and use the full scope of the instant claimed invention without undue amount of experimentation, the Office would require appropriate disclosure, in the way of scientifically sound reasoning or the way of concrete examples, as to why the data shown is a reasonably representative and objective showing such that it was commensurate in scope with and, thus, adequately enables, the use of these compounds for the full scope of the presently claimed subject matter. In the absence of such guidance and evidence or reasoning, the specification fails to provide an enabling disclosure.

Claim Rejections - 35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

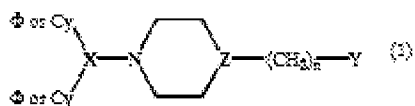
A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

21. Claims 1-4, 6, 7, 14, 15, and 17 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Snutch, USPT 6,387,897.

22. The claims of the instant application are drawn to methods of modulating (defined in the specification as inhibiting or increasing, see page 3, lines 11-12) human N-type calcium channel $\alpha_{1B} + \text{SFVG}$ subunit activity.

23. Snutch teaches that the administration of compounds of formula (1)



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can be used to inhibit N-type calcium channel activity. The compounds of formula (1) encompass the broad genus of claims 1, 2, 7, 15, and 17, as well as the elected species of claim 14. Snutch provides for methods of treating conditions associated with calcium channel activity comprising administering a compound of formula (1) or salts thereof. Upon administration of the compound, the calcium channel activity is inhibited, which falls within the definition of “modulating” of the instant specification.

24. Although Snutch does not specifically recite the modulation of the N-type calcium channel $\alpha_{1B+SFVG}$ subunit, it would be inherent that this particular subunit would be modulated by the compounds of Snutch since the compounds of both inventions are the same compounds. This would hold true whether it was known at the time of Snutch’s invention or not.

25. It is noted that In re Best (195 USPQ 430) and In re Fitzgerald (205 USPQ 594) discuss the support of rejections wherein the prior art discloses subject matter which there is reason to believe inherently includes functions that are newly cited or is identical to a product instantly claimed. In such a situation the burden is shifted to the applicants to “prove that subject matter shown to be in the prior art does not possess characteristic relied on” (205 USPQ 594, second column, first full paragraph).

26. Additionally, since the compounds of Snutch are the same compounds as the compounds of instant claimed invention, the properties laid forth in claims 4 and 6 would inherently be those of the compounds of Applicants invention.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shelley R. Graham whose telephone number is 571-270-1563. The examiner can normally be reached on M-R 9am-3pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

SRG
19 Nov 2007

/Cecilia Tsang/

Supervisory Patent Examiner, Art Unit 4173